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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/030,061	02/25/1998	MATTHEW TODD GILLSPIE	GILLISPIE-1	6893
1444	7590	01/06/2004	EXAMINER	
BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303			JIANG, DONG	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 01/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/030,061

Applicant(s)

GILLSPIE ET AL.

Examiner

Dong Jiang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-33, 35 and 36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 29-33, 35 and 36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's amendment filed on 07 October 2003 is acknowledged and entered. Following the amendment, claim 34 is canceled, and claim 33 is amended.

Currently, claims 29-33, 35 and 36 are pending and under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claim 34 are moot as the applicant has canceled the claim.

The objection of claim 35 is withdrawn in view of applicant's argument.

The rejection of claim 33 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 29-33, 35 and 36 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ushio et al., EP 0 712 931 A2, or Okamura et al., US 5,912,324 and further in view of Mark

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et al., US 4,588,585, for the reasons of record set forth in the previous Office Actions, paper Nos. 15, 17 and 22.

Applicants argument filed on 07 October 2003 has been fully considered, but is not deemed persuasive for reasons below.

At pages 6-8 of the response, the applicant argues that the Examiner's statement that it is well known in the art that cysteine residues in many protein molecules can be substituted or deleted without affecting biological activities of the proteins is not correct because cysteines may constitute an active center of a protein even if the cysteines are not involved in a disulfide bond. Applicant further argues that it is necessary to know when deciding whether cysteines give more stability to a protein: A. the position of cysteines in a protein; B. the involvement in disulfide bond; and C. whether constituting an active center if not involved in a disulfide bond. Furthermore, Applicant argues that the prior art references by Ushio and Okamura only provide information about A, but nothing about B and C in connection with IL-18, and the prior art reference by Mark provides information about A to C, but it is in connection with IL-2 and IFN-b, and therefore, information about B and C with regard to IL-18 was not available, thus, it would not have been obvious how to successfully stabilize IL-18 by replacing specific cysteines. This argument is not persuasive for the following reasons. First, the Examiner has never indicated that only cysteines that are involved in a disulfide bond are important and should not be deleted or replaced. As addressed in the previous Office Action, the knowledge in replacing certain cysteine residues while retaining biological activity of a protein, and its advantage in avoiding undesirable intermolecular or intramolecular structures are well known in the art. Therefore, the state of the prior art at the time the present invention was filed was high with the respect of cysteine substitutions/deletions, thus replacing/deleting certain cysteine residues of a protein, and testing for its functional activity to determine the importance of particular cysteine residues was is well within the skilled artisan's purview. Given the fact that Ushio and Okamura disclosed the sequence and the biological activity of the IL-18, the structural and functional relationship of the molecule can be determined by routine experimentation. Substituting/deleting cysteines of IL-18 and testing for its functional activity are considered routine, and obvious to a to person of ordinary skill in the art. The person of

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ordinary skill in the art reasonably would have expected success based on the structural and functional relationship of the IL-18 determined using the prior art disclosure. As the claims are not limited to particular location in the protein, they do not distinguish over the prior art.

Conclusion:

No claim is allowed.

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Advisory Information:

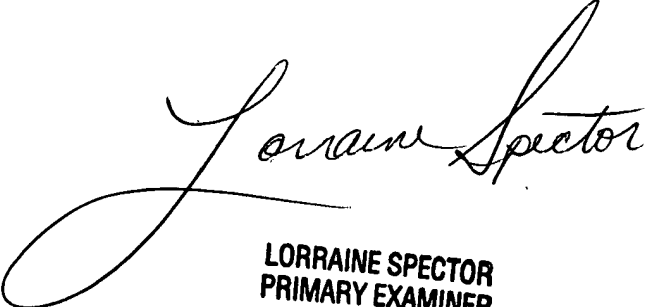
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


**LORRAINE SPECTOR
PRIMARY EXAMINER**

Dong Jiang, Ph.D.
Patent Examiner
AU1646
12/19/03